REMARKS

Claims 50-59 were pending in the subject application. By this amendment, applicants have canceled Claims 51-53 and 57-58 without prejudice or disclaimer, amended Claims 55-56, and added new Claims 60-64. Accordingly, upon entry of this amendment, claims 50, 54-56, and 59-64 will be pending and under consideration. Applicants maintain that the amendments to the claims do not raise an issue of new matter. Support for the amendments can be found at least in Claims 50-59. Accordingly, entry of the amendments is respectfully requested.

Summary of Attorney-Examiner Telephonic Interview

A telephonic interview was conducted on January 27, 2005 between Examiners Anne Marie Wehbe and Robert M. Kelly and attorneys Craig Arnold and Alan Miller. Applicants thank the Examiners for the courtesy of the interview.

The interview focused on the reasons for the outstanding written description and enablement rejections under 35 U.S.C. §112, first paragraph, on Declarations submitted by the inventors on May 20, 2003 and April 27, 2004, on additional information that applicants could provide to overcome the outstanding rejections, and on amendments that could be made to the claims.

It was agreed that applicants would submit for the Examiner's further consideration a reply that includes evidence that the SK3 and Kv1.5 potassium channel proteins, which are discussed in the May 20, 2003 Inventor's Declaration, were known in the art at the time the subject application was filed.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 50-54 and 58-59 are rejected under the written description and enablement requirements of 35 U.S.C. §112, first paragraph.

Applicants respectfully traverse these rejections.

Written Description Requirement

The application provides a teaching of using gene therapy for regulating corporal smooth muscle cells (See, page 17, lines 16 to 24; Claim 4 as filed). In addition, the application provides a teaching of using DNA encoding potassium channels proteins to induce relaxation of smooth muscle (See, page 19, lines 10-19; page 20, lines 5-6; Claim 8 as filed). With respect to relaxation of corporeal smooth muscle, the application as filed provides two specific examples of potassium channels, namely maxi-K and K_{ATP}, that can be introduced exogenously using gene therapy to induce relaxation of corporeal smooth muscle. In addition, the specification is replete with numerous references to the use of exogenous potassium channels in connection with corporeal smooth muscle and for the treatment of erectile dysfunction. By way of example, the specification teaches at page 21, lines 11-21, that regulating penile smooth muscle includes the introduction and expression of a DNA sequence encoding a protein involved in the regulation of smooth muscle tone, and at page 19, lines 10-17, page 20, lines 5-6, and Claim 8 as filed, potassium channels are provided as proteins involved in the regulation of smooth muscle tone. In addition, at page 27, lines 16-19, the specification teaches that "[p]otassium channels are important in the regulation of human smooth muscle tone." The specification also teaches that the "existence of such a diverse repertoire of K^+ channels has potentially-important implications for the modulation of electrical activity in human smooth muscle cells, including corporal myocytes." (See, page 27, lines 21-24). The

specification further teaches at page 78, lines 23-27 in the context of erectile and bladder physiology that "[t]he goal of gene therapy is . . . to restore a more normal balance between contracting and relaxing stimuli following expression of (an) exogenous gene(s) that code(s) for physiologically-relevant proteins in smooth muscle (e.g., the maxi-K channel or K_{ATP})." The present application further teaches that "[g]enes for more than thirty K^+ channels, many of which are expressed in smooth muscle, have been identified." (See, page 27, lines 16-19).

On May 20, 2003, applicants submitted a Declaration of Dr. George J. Christ under 37 C.F.R. §1.132 in which Dr. Christ presented evidence documenting the effectiveness in relaxing penile smooth muscle of two potassium channel proteins in addition to maxi-K and K_{ATP}, i.e., the voltage-dependent potassium channel protein Kv1.5 and the small-conductance, calcium-sensitive potassium channel protein SK3. Applicants attach hereto examples of references that demonstrate that these two potassium channel subtypes were known in the art before the February 13, 1997 priority date for the subject application, i.e.:

(1) Köhler, M et al. Small-conductance, calcium-activated potassium channels from mammalian brain. Science 273(5282):1709-14, 1996; and

(2) Malayev, AA et al. Mechanism of clofilium block of the human Kv1.5 delayed rectifier potassium channel. Mol. Pharmacol. 47(1): 198-205, 1995.

Applicants would also like to refer the Examiner to the Declaration of Drs. George J. Christ and Arnold Melman under 37 C.F.R. §1.132, filed on April 27, 2004. In their

Declaration, Drs. Christ and Melman discuss the meaning of the sentence spanning pages 27-28 of the specification. In particular, in paragraph 5 of the Declaration, Drs. Christ and Melman state that "This sentence was meant to characterize the state of the art, and more specifically, the physiological importance of endogenous maxi-K and KATP, based on pre-existing experimental and clinical data. This sentence was not meant to limit the invention, which relies on the use of nucleic acid encoding exogenous potassium channels to regulate corporal smooth muscle tone. Again, maxi-K and K_{ATP} are provided in the application as examples of exogenous potassium channels that can be used to regulate corporal smooth muscle tone." Earlier in the Declaration, in paragraph 4, Drs. Christ and Melman state that "As of the filing date of the application, the inventors considered their invention to include the use of a nucleic acid encoding an exogenous potassium channel generally for regulating corporal smooth muscle tone, and the use of nucleic acid encoding exogenous potassium channel subtypes maxi-K and K_{ATP} were provided as specific examples."

Applicants note that the sentence bridging pages 27-28 of the application is a discussion of the significance of maxi-K and K_{ATP} based upon an interpretation of the studies listed at the end of the sentence, namely Dorschner et al. (1999), Lee et al. (1999) and Benevides et al. (1999). Copies of these references were included with applicants' October 29, 2002 reply. Dorschner et al. studied the effects of hypoglycemic sulfonylureas on K_{ATP} channel subtypes in transfected COS-7 cells. Lee et al. characterized the K_{ATP} subtypes present in human corporal smooth muscle cells. Lee et al. state that "[a]mong the several subtypes of potassium channels present in smooth muscle, the calcium-sensitive (K_{Ca}; or maxi-K channel) and K_{ATP} channel subtypes are thought to be among the most important modulators of human corporal smooth muscle tone." (Emphasis added; Lee et al., p. 179, right column). Lee et al. go on to state that

"there has been no rigorous characterization of the K^+ channel subtype(s) that might be responsible for mediating these relaxing effects of the K channel modulators/openers in human corpora." (Lee et al., page 187, left column, first full paragraph.) Benevides et al. report the effects of intracavernosal injection of a potassium channel opener on erectile dysfunction. Thus, none of these references teach that the K_{ATP} and maxi-K channels are the only two K^+ channels that are relevant in the context of the claimed invention.

Applicants maintain that the claimed invention is described in the specification in sufficient detail that one skilled in the art can reasonably conclude that the inventors had possession of the claimed invention. Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

Enablement Requirement

The application as filed also provides an enabling disclosure for using DNA encoding potassium channels for inducing relaxation of corporeal smooth muscle. In this regard, the application provides two working examples demonstrating that DNA encoding maxi-K and K_{ATP}, when introduced and expressed in corporeal smooth muscle, are capable of inducing relaxation of corporeal smooth muscle. Applicants have also provided evidence that two additional potassium channel proteins known in the art at the time the subject application was filed, namely the voltage-dependent potassium channel protein Kv1.5 and the calcium-sensitive potassium channel protein SK3, are effective at inducing relaxation of corporeal smooth muscle. The present application further teaches that "[g]enes for more than thirty K^+ channels, many of which are expressed in smooth muscle, have been identified." (See, page 27, lines 16-19). Examples of nucleic acid sequences encoding potassium channel subtypes were included as an Exhibit in applicants' October 29, 2002 reply. Using the specific teachings of the

application, including the teachings of the working examples with DNA encoding maxi-K and K_{ATP}, the skilled artisan could readily prepare and introduce DNA encoding a potassium channel of interest into a corporeal smooth muscle, and determine whether the expressed potassium channel induces relaxation of the corporeal smooth muscle. Accordingly, reconsideration and withdrawal of this ground of rejection are respectfully requested.

Replacement of Information Disclosure Statement Form

In the current Office Action, the Examiner indicated that applicants' July 8, 2004 Information Disclosure Statement has been considered, but that the reference numbers "XP00....." could not be listed on a patent that issues from the subject application. Applicants attach hereto a replacement Form PTO/SB/08B from which such reference numbers have been deleted.

CONCLUSIONS

In view of the amendments and remarks made herein above, reconsideration and withdrawal of the rejections in the December 29, 2004 Office Action and passage of the pending claims to allowance are respectfully requested. If there are any minor matters that prevent allowance of the subject application, applicants request that the Examiner telephone the undersigned attorneys.

No fee is deemed necessary in connection with the submission of this reply. However, if there are unanticipated fees required to maintain the pendency of this application, the PTO is authorized to withdraw those fees from Deposit Account 01-1785.

Respectfully submitted,

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